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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/101,283 01/18/98 FISHER S 02307E-06001

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LAW OFFICES OF JONATHAN ALAN QUINE
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EXAMINER

JOHANSEN, D	
ART UNIT	PAPER NUMBER

1655
DATE MAILED: 10/03/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/101,283

Applicant(s)

FISHER ET AL.

Examiner

Diana B. Johannsen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 July 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-22 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Notice to Comply

DETAILED ACTION

1. This application has been transferred from Examiner Scott Houtteman in Art Unit 1656 to Examiner Diana Johannsen in Art Unit 1655. The amendment filed July 11, 2001, paper no. 14, has been entered. However, in view of prosecution by Examiner Johannsen, the prior Office action of paper no. 10 is withdrawn, and restriction is required as set forth below. It is noted that a non-final Office action on the merits will be prepared in response to applicants' election of one of the inventions set forth below.

Election/Restriction

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-2, drawn to proteins.

Group II, claim(s) 1 and 3, drawn to proteins.

Group III, claim(s) 1 and 4, drawn to proteins.

Group IV, claim(s) 5-6 and 17-18, drawn to methods of culturing cells.

Group V, claim(s) 7-9, drawn to methods of detecting hypoxic cells by detecting release of proteins.

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Group VI, claim(s) 7 and 10, drawn to methods of detecting hypoxic cells by detecting release of mRNA.

Group VII, claim(s) 11-13, drawn to methods of detecting abnormal placental function in a mammal.

Group VIII, claim(s) 14-15, drawn to methods of screening comprising assaying cell invasiveness.

Group IX, claim(s) 14 and 16, drawn to methods of screening comprising measuring protein release.

Group X, claim(s) 19-20, drawn to methods of detecting proteins indicative of metastasis.

Group XI, claim(s) 21-22, drawn to methods of identifying proteins indicative of an abnormal maternal placental interface.

3. The inventions listed as Groups I-XI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Groups I-III are each drawn to proteins. However, each of the claims sets forth multiple distinct proteins, each of which has different structural and functional characteristics. For example, proteins A-H differ from each other in having different molecular weights and different pIs. The proteins of claim 1(i)-claim 1(p) have different sequences and different functional properties. Accordingly, the different proteins recited in Groups I-III do not share any technical feature with each other that might constitute a shared special technical feature as required by PCT Rule 13.2.

It is further noted that the recitation of several distinct proteins in each of claims 1-4 is improper, as each of the recited proteins is distinct. Accordingly, the claims are in an improper Markush format (see *Ex parte Markush*, 1925 C.D. 126 and *In re Weber*,

198 USPQ 328). The different proteins are not obvious over one another, and a reference against any one of the recited proteins would not be a reference against any other of the recited proteins. Thus, the various Markush group members recited in claims 1-4 are not proper species. If applicant elects any of Groups I-III, applicant is further required to elect a single distinct protein. This is not an election of species. Should applicant traverse on the grounds that the different recited proteins constitute species that are not distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 USC 103(a) of the other invention. It is also noted that claim 1 has been included in multiple groups, as each of claims 2-4 recites a subset of the distinct proteins recited in claim 1. If any of Groups I-III is elected, claim 1 will be examined only as it reads upon the elected invention.

With respect to the relationship of the proteins of Groups I-III to the methods of Groups IV-XI, a shared technical feature is present in that the proteins of Groups I-III may be expressed by the cells employed in the methods of Groups IV-XI. However, the first product recited in Group I is "Protein A having a molecular weight of about 21 kDa and a pI of 6.0." The prior art as exemplified by Lifsey, Jr. et al (Biology of Reproduction 40:343-352 [1989]) discloses a bovine trophoblast protein meeting the limitations of "Protein A" of claim 1 (see entire reference). Accordingly, "Protein A" cannot constitute a special technical feature as defined by PCT Rule 13.2. Further, each of the proteins

of Groups I-III may be used in a variety of methods distinct from those of Groups IV-XI, including, e.g., methods of producing antibodies, methods of screening for protein-protein interaction, etc.

Each of the methods of Groups IV-XI also shares a technical feature because common proteins may be expressed by the cells employed in each of the methods. However, as discussed above, a protein meeting the limitations of the first recited protein is known in the art, and therefore a special technical feature as required by PCT Rule 13.2 is lacking. Further, the methods of each of Groups IV-XI have different objectives and require different reagents and different steps. For example, the method of Group IV require a step of culturing cells under hypoxic conditions to achieve the objective of culturing cells. The method of Group V requires a step of measuring release of a protein to achieve the objective of detecting hypoxic cells. The method of Group VI requires a step of measuring release of mRNA to achieve the objective of detecting hypoxic cells. The method of Group VII requires analyzing a sample from a mammal to achieve the objective of detecting abnormal placental function. The method of Group VIII requires a step of assaying cell invasiveness to achieve the objective of screening. The method of Group IX requires a step of measuring protein levels to achieve the objective of screening. The method of group X requires steps of raising cytotrophoblasts under hypoxic conditions and detecting novel proteins to achieve the objective of identifying proteins that are indicative of metastasis. The method of Group XI requires a step of detecting proteins to achieve the objective of identifying novel proteins that are indicative of an abnormal maternal placental interface.

It is further noted that applicant has presented several method claims in improper Markush format (see *Ex parte Markush*, 1925 C.D. 126 and *In re Weber*, 198 USPQ 328). With respect to claim 7, methods requiring detection of proteins (see dependent claims 8-9) and nucleic acids (see dependent claim 10) are improperly joined. Proteins and nucleic acids differ in both structure and function, and their detection requires different and unrelated method steps. Further, a reference against one method would not be a reference against the other. Accordingly, claim 7 has been included in both Group V and Group VI, and if either of those Groups is elected, will be examined only as it reads upon the invention of the elected Group. With respect to claim 14, methods requiring detection of cell invasiveness (see dependent claim 15) and detecting of levels of release of proteins (see dependent claim 16) are improperly joined. These methods require the use of different reagents and the performance of fundamentally different steps. Accordingly, claim 14 has been included in both Group VIII and Group IX, and if either of those Groups is elected, will be examined only as it reads upon the invention of the elected Group.

Additionally, the methods of Groups IV-VII each encompass detection of several distinct proteins and mRNAs encoding those proteins. As each of the recited proteins and mRNAs is distinct, the claims of these Groups are in an improper Markush format (see *Ex parte Markush*, 1925 C.D. 126 and *In re Weber*, 198 USPQ 328). The different proteins and mRNAs are not obvious over one another, and a reference against any one of the recited molecules would not be a reference against any other of the recited molecules. Thus, the various Markush group members recited in Groups IV-VII are not

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proper species. If applicant elects any of Groups IV-VII, applicant is further required to elect a single distinct protein (for Groups IV, V, or VII) or mRNA (Group VI). This is not an election of species. Should applicant traverse on the grounds that the different recited molecules constitute species that are not distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 USC 103(a) of the other invention.

4. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Sequence Listing

6. The communication filed August 31, 2000 is not fully responsive to the Office communication mailed May 16, 2000 for the reasons set forth on the attached Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Particularly, the Sequence Listing provided

by applicant is incomplete. For example, the Sequence Listing includes only SEQ ID Nos 1-18, whereas the specification also includes, e.g., SEQ ID NOS 19-20 (see, e.g., p. 40 of the specification). Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

The above-mentioned reply appears to be a *bona fide* attempt to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Applicant must correct the deficiencies in the Sequence Listing within the period for reply to this Office Action.

Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:00 am-3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/305-3014 for regular communications and 703/305-4242 for After Final communications.


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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen
September 28, 2001


W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

1011/01

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: Sequence Listing is incomplete.

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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